Remarks / Arguments

I.

Statement of the Substance of the Interview

Applicant thanks the examiner for the telephonic interview conducted on April 20, 2009 with applicant's representative, Raymond Wagenknecht. During the interview distinctions between claim 79 and the Cohen et al. reference were discussed. Specifically, the photoreactive group of the blocking reagent with respect to claim 79 was discussed in comparison to the photoreactive group of the crosslinking agent in Cohen et al. No final decision was reached; however, formally submitted arguments would be considered.

During the interview R. Wagenknecht set forth a position that in Cohen et al. the photoreactive group forms part of the initial crosslinking agent, which is layered over the substrate, but does not form part of the blocking reagent. It was clarified that although the crosslinking agent attaches to the blocking reagent, attachment occurs at the photoreactive group and thus once attached the crosslinking agent would no longer be photoreactive. It was further set forth that a photoreactive group must be by definition photoreactive.

In addition, R. Wagenkencht noted that the specification doesn't explicity state that attachment of the crosslinking agent to substrate occurs through a photoreactive group; however, even if the the crosslinking agent included two photoreactive groups, since the reactions would occur during the same irradiation step, it was consistent that attachment of the crosslinking agent to the substrate and to the blocking reagent would be simultaneous. As such, this would also eliminate the photoreactivity of a functional group that bonds to the substrate. Thus, it was set forth by R. Wagenknecht that Cohen et al. does not provide a blocking reagent having a photoreactive group for covalent immobilization.

II.

Restriction / Election

For completeness, claims 83, 84 and 86-91 are canceled as being directed towards the unelected invention.

III.

Introduction to the Invention

The present invention provides a blocking reagent having at least one photoreactive group for covalent immobilization on a sensor surface. Since the blocking reagent itself includes a photoreactive group for immobilization, the blocking reagent may be bound on the sensor surface without an intermediate crosslinking layer. Further, since a crosslinking layer is no longer required traditional masking techniques that selectively expose portions of the crosslinking layer for irradiation are also no longer required.

Formation of an exemplary blocking reagent is provided in example 1 and its immobilization on a sensor surface is provided in example 2. Notably in example 1, casein is reacted in the dark with a crosslinker (5-azido-2-nitrobenzoic acid N-hydroxysuccinimide ester in 20 molar equivalents of DMF). After which, the protein is purified and the pH of the solution adjusted. The blocking reagent, which includes the photoreactive group, is then applied to a sensor surface and irradiated with UV light for covalent immobilization. This is demonstrated in Example 2.

IV.

Claims 79-80 Are Not Anticipated Under 35 U.S.C. § 102 by Cohen et al. (US 2003/0207258) in light of Kamb et al. (US 2003/0027214)

The examiner rejects claims 79-80 under 35 U.S.C. § 102(e) as being anticipated by Cohen et al. (US 2003/0207258) in light of Kamb et al. (US 2003/0027214). Specifically, the examiner argues Cohen et al. teach a blocking reagent that attaches to a

crosslinking reagent, which includes a photoreactive group. The examiner adds that Kamb et al. teach a covalent bond formed between a photoreactive SANPAH and substrate when SANPAH is photoactivated.

A. Standard for Anticipation

Anticipation requires a single prior art reference disclose each and every element of the claim under consideration." W.L. Gore & Assocs. V. Garlock, Inc., 220 USPQ 303, 313 (Fed. Cir.1983). However, it is not enough that the reference discloses all of the claimed elements in isolation. Rather, as stated by the Federal Circuit, the prior art reference must disclose each and every element of the claimed invention "arranged as in the claim." Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co., 221 USPQ 481, 485 (Fed. Cir.1984). Further, the prior art must be such that a person of ordinary skill in the art would consider there to be no difference between the claimed invention and the referenced disclosure. In re Gurley, 31 USPQ2d 1130, 1132 (Fed Cir. 1994).

B. Claims 79 and 80 provide a blocking reagent having a photoreactive group for covalent immobilization on a sensor surface; whereas Cohen et al. provide a crosslinking agent with a photoreactive group for attachment to a blocking reagent, which upon attachment is no longer photoreactive

In claims 79-80, the blocking reagent has at least one photoreactive group for covalent immobilization on a sensor surface. Since the blocking reagent itself has a photoreactive group, its immobilization does not require layering a crosslinking agent over the sensor and does not require masking to selectively irradiate portions of a crosslinking layer.

In contrast, Cohen et al. teach a crosslinking agent that includes a photoreactive group that attaches covalently to a blocking material. However, once covalently attached, the group is no longer photoreactive. Thus the result is a blocking reagent without a photoreactive group. Cohen et al. is now discussed in more detail.

Cohen et al. coat a substrate with a crosslinking agent, which includes a first functional group for attachment to the substrate and a second functional group for attachment to molecules, such as a blocking material. The two functional groups are structurally distinguished. Although features of the first functional group are not explicitly provided, the second functional group, which attaches to the block material, is described as photoreactive. This is summarized in paragraph [0030], which provides,

> "A layer containing a photo-reactive crosslinking agent is first applied to a surface of the substrate member. The molecular structure of the crosslinking agent is such that one functional group or side thereof reacts with or attaches to the surface of the substrate member. Another functional group or side of the crosslinking agent is photoactivatable such that, in the presence of the correct amplitude and frequency of electromagnetic radiation, the group will cross-link with other molecules in close proximity. Specifically, the photo-reactive crosslinking agent may be any one of a number of substances, including SANPAH (N-Succinimidyl 2-[pazido-salicylamido] ethyl-1, 3'-dithiiopropionate); SAND (Sulfosuccinimidyl 2[m-azido-o-nitro-benzamido] ethyl-1, 3'-dithiopropionate); and ANB-NOS (N-5-Azido-2-nitrobenzoyloxysuccinimide-)." (emphasis added)

After coating the substrate with the crosslinking agent a coating of blocking material is applied. The substrate is selectively masked and irradiated with an energy source to activate the photoreactive group of the crosslinking agent. This is summarized at paragraph [0031], which provides,

> "A generally uniform coating of the receptive material or the blocking material is then applied to the substrate surface over the crosslinking agent layer. A mask is placed over the substrate, and the mask and substrate combination is irradiated with an energy source specifically selected to activate the photo-reactive group of the crosslinking agent. In its basic form, the "mask" serves to shield at least one area or section of the substrate member from the irradiating energy source and to expose at least one adjacent section to the energy source." (emphasis added)

Once the photoreactive group is activated, it attaches to the blocking material. This is summarized at paragraph [0032], which provides.

> "As mentioned, the energy source is selected so that the reactive group of the exposed crosslinking agent is activated and thus attaches or crosslinks with the overlying material (the receptive material or blocking material)."

Thus, in Cohen et al. the photoreactive group of the crosslinking agent is activated for attachment to the blocking material. However, after attachment to the blocking material the crosslinking agent is no longer photoreactive. In other words, additional irradiation will not activate the same crosslinking agent. This is further supported by the next step in Cohen et al., which is to unmask the substrate, apply the receptive material (capture molecules) and photoactively crosslink the receptive material without remasking the substrate. In other words, since the crosslinked blocking material is not photoreactive there is no need to mask the substrate a second time. Only previously shielded areas of the crosslinking layer remain photoreactive. This second irradiation step is disclosed at paragraphs [0033] and [0034], which provide,

> "The receptive material or blocking material that was under the shielded areas of the mask (and thus not crosslinked with the crosslinking agent) is removed from the substrate in any suitable cleansing process, such as rinsing the substrate with water or a buffer solution.
>
> A generally uniform layer of the respective other material is then applied to the substrate member... if the blocking material was first applied, the receptive material is subsequently applied. The substrate member is then exposed to the energy source a second time so as to activate the remaining crosslinking agent in the areas of the substrate member that were shielded by the mask in the masking process. . .. Any remaining un-linked material is then cleaned from the substrate member in an appropriate cleaning process, e.g., a rinsing step." (emphasis added)

Therefore, although the crosslinking agent in Cohen et al. initially includes a photoreactive group, the photoreactive group bonds with the blocking material, which causes the crosslinking agent to lose its photoreactivity. Accordingly, when attached to the crosslinking agent the blocking material is not photoreactive. This is specifically demonstrated in Cohen et al. As such, Cohen et al. does not anticipate claims 79-80 and applicant requests the rejections be withdrawn.

C. Cohen et al. CAN NOT include a blocking reagent having at least one photoreactive group for covalent immobilization on a sensor surface because irradiation initiates bonding at all unshielded photoreactive groups simultatenously

Although Cohen et al. only indicate the second functional group is photoreactive, applicant also discusses the implications of two photoreactive groups, one for attachment to the substrate surface and one for attachment to the blocking reagent.

Before considering a crosslinker with two photoreactive groups, it is noteworthy that it is more consistent with the specification that each crosslinking agent only includes one photoreactive group. For instance, only the second group is described as photoreactive. This is exemplified in paragraph [0030], which provides,

> "The molecular structure of the crosslinking agent is such that one functional group or side thereof reacts with or attaches to the surface of the substrate member. Another functional group or side of the crosslinking agent is photoactivatable such that, in the presence of the correct amplitude and frequency of electromagnetic radiation, the group will cross-link with other molecules in close proximity." (emphasis added)

This interpretation of Cohen et al. is also consistent with paragraph [0031], which uses the singular term "functional group" instead of the plural "functional groups" when referring to photoreactivity, "the mask and substrate combination is irradiated with an energy source specifically selected to activate the photo-reactive group of the crosslinking agent."

Thus, the language of the specification suggests the two functional groups are not identical, namely only the second group is photoreactive. As discussed above, once attached to the blocking reagent, the crosslinking agent is no longer photoreactive. However, for completeness two photoreactive groups are also considered.

Even if the teachings of Cohen et al. are interpreted as providing two photoreactive groups, one for attachment to the blocking material and one for attachment to the substrate, irradiation would activate both functional groups simultaneously. Thus, attachment of the crosslinking agent to the substrate and to the blocking material by photoreactive groups would occur simultaneously. Accordingly, even if both functional groups were photoreactive, Cohen et al. would still not teach a blocking reagent having a photoreactive group for covalent immobilization on a sensor surface. Instead, Cohen et al. would provide an immobilized blocking reagent without a photoreactive group. As

such, Cohen et al. does not demonstrate a blocking reagent having at least one photoreactive group for covalent immobilization on a sensor surface.

Since Cohen et al. can not provide a blocking reagent with a photoreactive group, Cohen et al. does not anticipate the present invention. Accordingly, applicant respectfully requests the rejection be withdrawn and claims 79-80 allowed.

D. The difference in technical approaches between the blocking reagent of claims 79-80 and the crosslinking layer – blocking reagent of Cohen et al. further demonstrate significant differences between the inventions

Although the structural differences between the blocking reagent in claims 79-80 and Cohen et al. are demonstrated above, namely once the crosslinking agent layer in Cohen et al. covalently bonds with the blocking material the crosslinking agent layer is no longer photoreactive, the differences are also evident by comparing the technical approaches.

Since the blocking material in Cohen et al. requires binding to a crosslinking layer, technologically, Cohen et al. require the use of selective masking to define the receptive areas and blocking areas of the substrate. Referring to paragraphs [0030] – [0031],

> "The present invention comprises, in broad terms, a process of defining an active pattern of analyte-specific receptive material on a substrate surface by photo-masking the substrate. A layer containing a photo-reactive crosslinking agent is first applied to a surface of the substrate member..
>
> A generally uniform coating of the receptive material or the blocking material is then applied to the substrate surface over the crosslinking agent layer. A mask is placed over the substrate, and the mask and substrate combination is irradiated with an energy source specifically selected to activate the photo-reactive group of the crosslinking agent. In its basic form, the "mask" serves to shield at least one area or section of the substrate member from the irradiating energy source and to expose at least one adjacent section to the energy source." (Emphasis added)

The unmasked areas of the substrate are irradiated for selective binding of the first material. Specifically, irradiation activates the portion of the crosslinker that is exposed (or unshielded) by the mask. Referring to paragraph [0032],

> "As mentioned, the energy source is selected so that the reactive group of the exposed crosslinking agent is activated and thus attaches or crosslinks with the overlaying material (the receptive material or blocking material)." (Emphasis added).

After crosslinking the first material to the crosslinking layer, the mask is removed and the substrate is washed to remove unbound first material. Referring to paragraph [0033],

> "The receptive material or blocking material that was under the shielding areas of the mask (and thus not crosslinked with the crosslinking agent) is removed from the substrate in any suitable cleansing process, such as rinsing the substrate with water or buffer solution."

The second material is then added. The areas of the crosslinking layer that were previously shielded are then irradiated for binding to the second material. Referring to paragraph [0034],

> "A generally uniform layer of respective other material is then applied to the substrate member... The substrate member is then exposed to the energy source a second time so as to activate the remaining crosslinking agent in the areas of the substrate member that were shielded by the mask in the masking process." (Emphasis added)

Thus in Cohen et al. the photoreactive crosslinking layer and masking technique are used in combination to selectively bind the receptive material and blocking material in designated areas. The receptive areas and blocking areas are defined through the use of selective shielding by the mask and are thus spatially distinct. In other words, the masking permits the separation of receptive areas and blocking areas, each of which are bound to the photoreactive crosslinking layer.

In addition to selective masking, there is another important feature in Cohen et al. that should be specifically pointed out for comparison to Applicant's blocking reagent. In Cohen et al. the photoreactive crosslinking layer is activated by irradiation. Since the photoreactive crosslinking layer is activated and not the blocking material, there is little

concern with respect to design of the blocking material and therefore the blocking material itself includes no special technical features. Referring to paragraph [0016],

> "These "different" molecules will serve, in essence, to fill in or block the regions on the substrate between the active receptor material areas and may be, for example, biomolecules that specifically do not have affinity for the analyte of interest. In general, any type of blocking material may be used for this purpose." (Emphasis added)

Since Cohen et al. provides no special technical requirements or features of its blocking material, the blocking material provides no particular contribution to the state of the art.

With respect to claims 79-80, the blocking reagent itself includes a photoreactive group for covalent immobilization to the sensor, thus eliminating the need for a crosslinking layer and photomasking. In other words, the blocking reagent in claims 79-80 can covalently attach to the substrate without such a photoreactive crosslinking layer. Further, unlike in Cohen et al., the blocking reagent in claims 79-80 may also be applied within the detection region, which may be desirable to prevent or reduce nonspecific interactions within the detecting region of the sensor. The result is an improved signal to noise ratio.

Thus, in addition to the structural differences above, viewing the technological approaches as a whole further demonstrates Cohen et al. does not anticipate claims 79-80. Further, one skilled in the art would consider the blocking reagents themselves and the technical approaches significantly different. Accordingly, applicant respectfully requests the rejection be withdrawn.

V.
Response to Rejections Under 35 U.S.C. § 103
(Obviousness)

A. Standard for Obviousness

The examiner indicates a proper obviousness rejection requires consideration of the factual inquiries provided in Graham v. John Deere Co., 38 U.S. 1, 148 USPQ 459

(1966), including: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims at issue; 3) resolving the level of ordinary skill in the pertinent art; and 4) considering the objective evidence present in the application indicating obviousness or nonobviousness. However, although Graham v. John Deere requires that certain factual inquiries be conducted to support a determination of the issue of obviousness, the actual determination of the issue requires an elevation in light of the findings in those inquiries as to the obviousness *of the claimed invention as a whole*, not merely the differences between the claimed invention and the prior art. Lear Siegelr, Inc. v. Aeroquip Corp., 221 USPQ 1025, 1033 (Fed. Cir. 1984).

B. Claim 81 is not obvious over Cohen et al. (US 2003/020728) in light of Kamb et al. (US 2003/0027214) as applied to claim 80 and further in view of Caldwell et al. (US 5,516,703)

With respect to claim 81, the examiner argues that Cohen et al. in light of Kamb et al. teach a pluronic surfactant blocking reagent but fail to teach the surfactant specifically being PLURONIC F-68. However the examiner cites Caldwell et al. as teaching modified pluronic surfactants immobilized to a substrate, namely Pluronic F-68 in order to provide a surface with minimum non-specific binding.

The deficiencies of Cohen et al. in light of Kamb et al. are discussed above with respect to claim 79. Since claim 79 is not anticipated by Cohen et al. in light of Kamb et al. as demonstrated above, claim 81, which depends from claim 79, is not obvious over Cohen et al. in light of Kamb et al. and further in view of Caldwell et al.

Accordingly, applicant respectfully requests the rejection be w`ithdrawn and claim 81 allowed.

C. Claim 82 is not obvious over Cohen et al. (US 2003/0207258) in light of Kamb et al. (US 2003/0027214) and further in view of Pomato et al (US 5,5965,106)

With respect to claim 82, the examiner acknowledges Cohen et al in light of Kamb et al. fail to teach the photoreactive group of SANPAH being benzophenone. However, the examiner argues Pomato et al. teach a photoreactive benzophenone being advantageous over a photoreactive group of arylazide reagents, wherein SANPAH is an arylazide reagent , in order to provide an in vivo delivery system that is easily synthesized and purified in high yields.

The deficiencies of Cohen et al. in light of Kamb et al. are discussed above with respect to claim 79. Since claim 79 is not anticipated by Cohen et al. in light of Kamb et al. as demonstrated above, claim 82, which depends from claim 79, is not obvious over Cohen et al. in light of Kamb et al. and further in view of Pomato et al.

Accordingly, applicant respectfully requests the rejection be withdrawn and claim 82 allowed.

VI.

Conclusion

In view of the arguments set forth above, applicant respectfully requests the rejections be withdrawn and all claims allowed.

Respectfully submitted,

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Date

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